REMARKS

Entry of the foregoing and reexamination and reconsideration of the subject application, as amended, pursuant to and consistent with 37 C.F.R. § 1.112, are respectfully requested in light of the remarks which follow.

Applicants thank Examiner Kam for discussing the outstanding claims with Applicants' representative on August 1, 2005.

As noted in the Office Action Summary, claims 54-98 are pending. Claims 54, 61-64, 66 and 73 are amended herein; claims 56-60, 65, 67, 72, 74 and 98 are canceled; and new claims 99-109 are added. Claim 61 is amended to appear in independent form. Basis for the amendments and for the new claims may be found throughout the specification and claims as-filed. Applicants reserve the right to file at least one continuation or divisional application directed to any subject matter canceled by way of the present Amendment. No new matter is presented by way of the present Amendment.

Rejections Under 35 U.S.C. § 102

Claims 54, 56-60, 75, 77-85, 87, and 91-96 stand rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Tomita. Tomita purportedly discloses a microbial peptide with a sequence of Ala-Thr-Lys-Cys-Phe-Gln-Trp-Gln-Arg-Asn-Met-Arg-Lys-Val-Arg-Gly-Pro-Pro-Val-Ser-Cys-Ile-Lys-Arg-Asp. The sequence of Tomita is alleged to fall within the penumbra of SEQ ID NO:99, having the Thr-Lys at the amino terminus, Gly-Pro-Pro-Val-Ser-Cys-Ile-Lys-Arg at the carboxy terminus, and is not SEQ ID NO:38. Applicants respectfully traverse.

To anticipate a claimed invention under §102, a reference must teach each and every element of the claimed invention. *See Lindeman Machinenfabrik GmbH v. American Hoist and Derrick Company*, 221 USPQ 481, 485 (Fed. Cir. 1984). Tomita does not recite each element of the present invention.

As amended herein, the present claims recite the following specific sequences: SEQ ID NOS. 2-5, 8, 31-37, 47, 49, 51, 63, 65, 67, 70, 72-74, 80-83, and 87-97. Tomita does not disclose these sequences. Thus, Tomita fails to recite each and every element of the claimed invention.

Attached hereto as Exhibit A is a sequence alignment, illustrating all of the sequences set forth in the presently amended claims. As shown, all of the sequences currently claimed are related and share amino acid sequences not found in the sequences of Tomita (as well as the other cited reference, Shimazaki, discussed below).

With regard to SEQ ID NOS:2 and 3, having 25 or more residues, Applicants submit that these sequences are different from those shown in Tomita. Applicants refer to the attached alignments shown in Exhibit A, showing the differences between the sequences of the claims and those of the cited references.

Applicants also provide the following comments as to the presently claimed sequences. SEQ ID NOS. 2-5 all share a common motif, that of SEQ ID NO:99, and have high sequence homology. These sequences are part of one larger embodiment, as seen on page 6, lines 1-3, of the specification. Thus, SEQ ID NOS:8-42 also belong to one embodiment (see page 8, lines 2-5). SEQ ID NO:8 and 31-37 share the motif of SEQ ID NO:99 and also exhibit high sequence homology. SEQ ID NO:67 corresponds to the capped version of SEQ ID NO:34, SEQ ID NO:63 corresponds to the capped version of SEQ ID NO:35, SEQ ID NO:51

corresponds to the capped version of SEQ ID NO:36, SEQ ID NO:49 corresponds to the capped version of SEQ ID NO:37 and SEQ ID NO:47 corresponds to the capped version of SEQ ID NO:38. Applicants further note that SEQ IS NOS:68-99 also belong to one embodiment (see page 10, lines 18-20 of the specification). Within these sequences, SEQ ID NOS:70, 72-74, 80-83, and 87-97 share a common motif set forth in SEQ ID NO:99 and have high sequence homology.

In addition, Applicants submit that the present invention is directed to peptides from human lactoferrin, having a therapeutic effect. These peptides, altered to have a therapeutic effect, are different from those sequences of the cited references. Not only do the cited references fails to disclose the sequences of the presently claimed invention, but they also fail to disclose how the skilled artisan may modify the sequences of the cited references in order to arrive at the presently claimed sequences. The cited references fail to disclose how the skilled artisan may modify the sequences set forth and arrive at a therapeutic effect. One of skill in the art may randomly modify the sequences disclosed in the references, but the chances of arriving at the peptide chain modifications that result in the presently claimed sequences are random at best.

The Office alleges that Tomita teaches that the "peptide can be formulated and administered to humans or animals and used in food product such as chewing gum or in medicinal products such as eye medications or athlete's foot medications." *See* col. 6, line 45 to col. 7, line 8 of Tomita.

In response, Applicants submit that Tomita is directed to antimicrobial peptides isolated from lactoferrin hydrolysate. These peptides contain some amino acid sequences that may appear to be similar to the present peptides but are not identical. Tomita discloses antimicrobial peptides, agents containing these peptides

as the active ingredient, and methods of using same. For example, Tomita discloses eyedrops, mouth washes, gum, antiperspirants, toothpastes, skin washes, flower preservatives, and an antifungal agent.

However, Tomita does not disclose or suggest the treatment and/or prevention of inflammation. There are no experiments, let alone disclosure, showing the *in vivo* administration of the peptides. There is no teaching in Tomita as to the administration for the treatment of a specific disease state. Instead, Tomita suggests the use of the peptides as useful on the surface of products, such as toilet paper and diapers, and in combination with other antimicrobial agents. Thus, Tomita is directed to preservative agents not to be administered to an animal or human to treat disease, but instead to be used to kill germs on a surface.

By way of support, attached as Exhibit B is data showing the positive therapeutic effects of the peptides of the present invention. As shown, rats given the peptides of the present invention showed marked improvement and reduction in abdominal adhesions following surgery.

Claims 54, 56-59, 65, 72, 74, 75, 77-85, and 98 stand rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Shimazaki. Shimazaki purportedly discloses the following two sequences:

Lys-Cys-Phe-Gln-Trp-Gln-Arg-Asn-Met-Arg-Lys-Val-Arg-Gly-Pro-Pro-Val-Ser-Cys-Ile

and

Val-Ser-Gln-Pro-Gly-Ala-Thr-Lys-Cys-Phe-Gln-Trp-Gln-Arg-Asn-Met-Arg-Lys-Val-Arg-Gly-Pro-Pro-Val-Ser-Cys-Ile-Lys-Arg-Asp-Ser-Prolle-Gln-Cys-Ile-Gly-Arg-Arg-Arg-Arg-Ser-Val-Gln-Trp-Cys-Ala.

Applicants submit that the full translation of Shimazaki, as provided by the Office, does not disclose each element of the present invention. As amended herein, the present claims recite the following specific sequences: SEQ ID NOs. 2-5, 8, 31-37, 47, 49, 51, 63, 65, 67, 70, 72-74, 80-83, and 87-97. Shimazaki does not disclose these sequences.

In light of the above, Applicants respectfully request that the rejections under 35 U.S.C. § 102 be withdrawn.

Rejections Under 35 U.S.C. § 112, second paragraph

Claims 61-64 stand rejected as purportedly indefinite, because allegedly these claims do not further limit Claim 55. Claims 61-63 are amended herein to recite specific sequences, as further limiting to base claim 55. Thus, this rejection is obviated.

Claim 67 stands rejected as purportedly indefinite for the recitation of "peptide comprises SEQ. ID NOS: 68, 69, 71, 75-79, and 84-86," as these sequences purportedly do not conform with SEQ ID NO:99. Claim 67 is canceled herein without prejudice or disclaimer thereto, and thus the rejection is moot.

In light of the above, Applicants respectfully request that the rejections pursuant to 35 U.S.C. § 112, second paragraph be withdrawn.

Claim Objections

Applicants note with appreciation that claims 55, 66, 68-71, 73, 76, 86, 88-90, and 97 would be allowable if rewritten as independent claims.

CONCLUSION

It is respectfully submitted that all rejections have been overcome by the above amendments. Thus, a Notice of Allowance is respectfully requested.

In the event that there are any questions relating to this amendment or the application in general, it would be appreciated if the Examiner would contact the undersigned attorney by telephone at (703) 836-6620 so that prosecution of the application may be expedited.

Respectfully submitted,

BUCHANAN INGERSOLL PC
(INCLUDING ATTORNEYS FROM BURNS, DOANE, SWECKER & MATHIS)

Date September 6, 2005

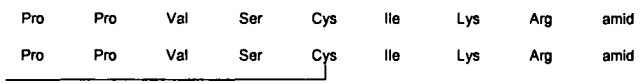
By: _____
Deborah H. Yellin
Registration No. 45,904

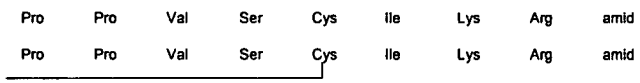
P.O. Box 1404
Alexandria, Virginia 22313-1404
(703) 836-6620

Lactoferrin sequence no:		12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	
parental sequence: seq id 99									Cys Cys	Phe Phe	Gln X1	Trp X2	Gln X3	Arg X4	Asn X5	Met X6	Arg X7	Lys Lys	Val Val	Arg Arg		
modifications:											Ala	Leu	Lys Orn Ala Nle	Lys Ala	Orn Ala Nle	Leu	Lys					
8		Val	Ser	Gln	Pro	Glu	Ala	Thr	Lys	Cys	Phe	Gln	Trp	Gln	Arg	Asn	Met	Arg	Lys	Val	Arg	
32			Ser	Gln	Pro	Glu	Ala	Thr	Lys	Cys	Phe	Gln	Trp	Gln	Arg	Asn	Met	Arg	Lys	Val	Arg	
33				Gln	Pro	Glu	Ala	Thr	Lys	Cys	Phe	Gln	Trp	Gln	Arg	Asn	Met	Arg	Lys	Val	Arg	
34					Pro	Glu	Ala	Thr	Lys	Cys	Phe	Gln	Trp	Gln	Arg	Asn	Met	Arg	Lys	Val	Arg	
67				acetyl-	Pro	Glu	Ala	Thr	Lys	Cys	Phe	Gln	Trp	Gln	Arg	Asn	Met	Arg	Lys	Val	Arg	amid
31						Glu	Ala	Thr	Lys	Cys	Phe	Gln	Trp	Gln	Arg	Asn	Met	Arg	Lys	Val	Arg	
65					acetyl	Glu	Ala	Thr	Lys	Cys	Phe	Gln	Trp	Gln	Arg	Asn	Met	Arg	Lys	Val	Arg	amid
seq no.: 2					acetyl-	Glu	Ala	Thr	Lys	Cys	Phe	Gln	Trp	Gln	Arg	Asn	Met	Arg	Lys	Val	Arg	Gly
3	disulphide 20-37				acetyl-	Glu	Ala	Thr	Lys	Cys	Phe	Gln	Trp	Gln	Arg	Asn	Met	Arg	Lys	Val	Arg	Gly
35							Ala	Thr	Lys	Cys	Phe	Gln	Trp	Gln	Arg	Asn	Met	Arg	Lys	Val	Arg	
63						acetyl-	Ala	Thr	Lys	Cys	Phe	Gln	Trp	Gln	Arg	Asn	Met	Arg	Lys	Val	Arg	amid
36								Thr	Lys	Cys	Phe	Gln	Trp	Gln	Arg	Asn	Met	Arg	Lys	Val	Arg	
51							acetyl-	Thr	Lys	Cys	Phe	Gln	Trp	Gln	Arg	Asn	Met	Arg	Lys	Val	Arg	amid
4							acetyl-	Thr	Lys	Cys	Phe	Gln	Trp	Gln	Arg	Asn	Met	Arg	Lys	Val	Arg	Gly
5	disulphide 20-37						acetyl-	Thr	Lys	Cys	Phe	Gln	Trp	Gln	Arg	Asn	Met	Arg	Lys	Val	Arg	Gly
37									Lys	Cys	Phe	Gln	Trp	Gln	Arg	Asn	Met	Arg	Lys	Val	Arg	
49								acetyl-	Lys	Cys	Phe	Gln	Trp	Gln	Arg	Asn	Met	Arg	Lys	Val	Arg	amid
47									acetyl-	Cys	Phe	Gln	Trp	Gln	Arg	Asn	Met	Arg	Lys	Val	Arg	amid
70										Cys	Phe	Ala	Trp	Gln	Arg	Asn	Met	Arg	Lys	Val	Arg	
72										Cys	Phe	Gln	Trp	Ala	Arg	Asn	Met	Arg	Lys	Val	Arg	
73										Cys	Phe	Gln	Trp	Gln	Ala	Asn	Met	Arg	Lys	Val	Arg	

EXHIBIT A
A.N. 09/743,107
Amdt filed 9/6/05

74		Cys	Phe	Gln	Trp	Gln	Arg	Ala	Met	Arg	Lys	Val	Arg	
80		Cys	Phe	Gln	Leu	Gln	Arg	Asn	Met	Arg	Lys	Val	Arg	
81		Cys	Phe	Gln	Trp	Gln	Lys	Asn	Met	Arg	Lys	Val	Arg	
82		Cys	Phe	Gln	Trp	Gln	Arg	Asn	Leu	Arg	Lys	Val	Arg	
83		Cys	Phe	Gln	Trp	Gln	Arg	Asn	Met	Lys	Lys	Val	Arg	
87		Cys	Phe	Gln	Trp	Orn	Arg	Asn	Met	Arg	Lys	Val	Arg	
88		Cys	Phe	Gln	Trp	Nle	Arg	Asn	Met	Arg	Lys	Val	Arg	
89		Cys	Phe	Gln	Trp	Gln	Arg	Orn	Met	Arg	Lys	Val	Arg	
90		Cys	Phe	Gln	Trp	Gln	Arg	Nle	Met	Arg	Lys	Val	Arg	
91		Cys	Phe	Gln	Trp	Lys	Arg	Asn	Met	Arg	Lys	Val	Arg	
92	acetyl-	Cys	Phe	Gln	Trp	Lys	Arg	Asn	Met	Arg	Lys	Val	Arg	amid
93		Cys	Phe	Gln	Trp	Lys	Arg	Ala	Met	Arg	Lys	Val	Arg	
94		Cys	Phe	Ala	Trp	Lys	Arg	Asn	Met	Arg	Lys	Val	Arg	
95		Cys	Phe	Ala	Trp	Gln	Arg	Ala	Met	Arg	Lys	Val	Arg	
96		Cys	Phe	Gln	Leu	Lys	Lys	Asn	Met	Lys	Lys	Val	Arg	
97		Cys	Phe	Ala	Leu	Lys	Lys	Ala	Met	Lys	Lys	Val	Arg	


Pro Pro Val Ser Cys Ile Lys Arg amid
Pro Pro Val Ser Cys Ile Lys Arg amid


Pro Pro Val Ser Cys Ile Lys Arg amid
Pro Pro Val Ser Cys Ile Lys Arg amid

APPENDIX 1

Lactoferrin based peptides – effect on abdominal adhesions

It has been understood that formation of abdominal adhesions following surgery is based on inflammatory changes in the peritoneum.

To assess the anti-inflammatory properties of lactoferrin and peptide derivates of lactoferrin a peritoneal injury (25x5 mm) was performed and sutured in anaesthetized rats. After 7 days, the distance of intestines that had adhered to the peritoneal injury was measured by calipers. This is a commonly used method to analyze the formation and degree of abdominal adhesions.

The rats were treated by daily intra peritoneal injections of distilled water at pH 6.9 (control), 10 mg of bovine lactoferrin, 1 mg or 0.1 mg of SEQ ID NO: 2, 1 mg of SEQ ID NO: 93, and 1 mg or 0.1 mg of SEQ ID NO: 37. The peptides were dissolved in distilled water at pH 6.9. The injected volume was always 0.1 ml.

The data are presented in the table. Lactoferrin at 10 mg/day induced a statistically significant reduction of abdominal adhesion formation, assessed by ANOVA-test (ANalysis Of VAriance). The reduction of adhesion formation was even more pronounced for SEQ ID NO: 2 at both 1 mg/day and 0.1 mg/day.

Group	n	Mean	Standard deviation	ANOVA
Control	17	16.1	8.0	-
Doxycyclin	10	10.9	7.9	0.0808
Infliximab	5	15.4	5.5	0.08586
Infliximab x2	10	7.9	6.0	0.0067*
Lactoferrin 10 mg	9	5.7	5.2	0.0010*
SEQ ID NO: 2 1 mg	6	3.0	3.5	0.0003*
SEQ ID NO: 2 0.1 mg	5	2.3	3.4	0.0003*
SEQ ID NO: 93 1 mg	6	9.2	8.6	0.0511
SEQ ID NO: 37 1 mg	5	7.6	11.2	0.0260*
SEQ ID NO: 37 0.1 mg	6	12.3	6.9	0.2829

The ANOVA results denoted by * represent statistically significant improvements over the control samples.